

Access DB#

89405

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name:

Kahsay Mbik

Examiner #: 78271

Date: Mar. 19, 2003

Art Unit: 1624

Phone Number 308-4717

Serial Number: 09/980,593

Mail Box and Bldg/Room Location: 4E-18

Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

MEJ

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

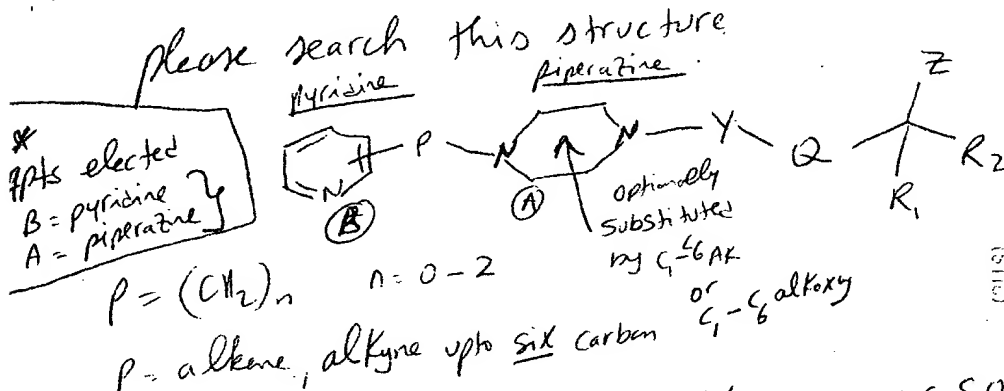
Title of Invention:

Inventors (please provide full names):

Earliest Priority Filing Date: 5/31/2000

* Please see attached

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



STAFF USE ONLY

Searcher: Skerjanc

Searcher Phone #: 308-4499

Searcher Location:

Date Searcher Picked Up:

Date Completed: 3/20/03

Searcher Prep & Review Time:

Clerical Prep Time:

Online Time:

Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#)

Bibliographic

Litigation

Fulltext

Patent Family

Other

Vendors and cost where applicable

STN

Dialog

Questel/Orbit

Dr. Link

Lexis/Nexis

Sequence Systems

WWW/Internet

Other (specify)

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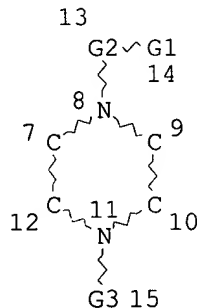
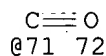
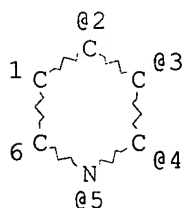
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FILE COVERS 1907 - 20 Mar 2003 VOL 138 ISS 12
FILE LAST UPDATED: 19 Mar 2003 (20030319/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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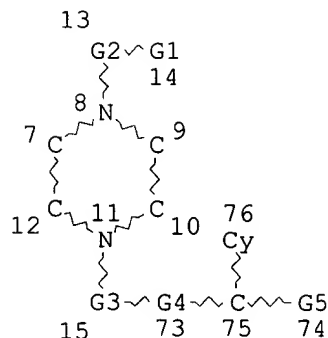
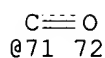
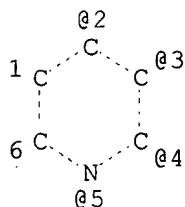
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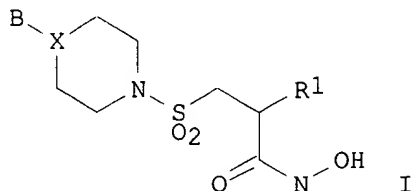
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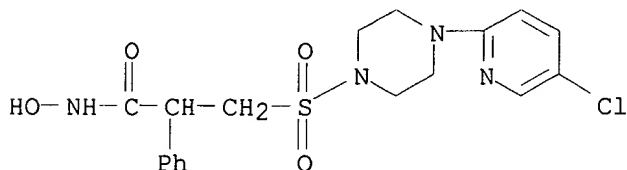
L16 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:636067 HCAPLUS
 DOCUMENT NUMBER: 135:195577
 TITLE: Preparation of arylpiperazines and arylpiperidines as metalloproteinase inhibiting agents
 INVENTOR(S): Barlaam, Bernard Christophe; Dowell, Robert Ian; Newcombe, Nicholas John; Tucker, Howard; Waterson, David
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062751	A1	20010830	WO 2001-GB616	20010215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

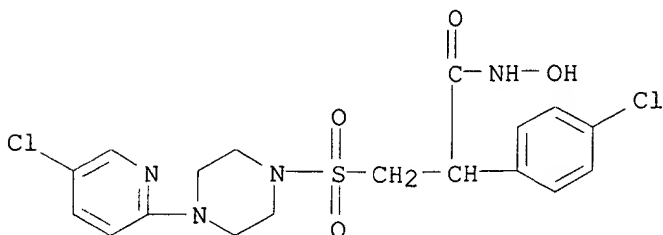
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 EP 1261595 A1 20021204 EP 2001-905883 20010215
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 NO 2002003951 A 20020820 NO 2002-3951 20020820
 PRIORITY APPLN. INFO.: EP 2000-400469 A 20000221
 WO 2001-GB616 W 20010215
 OTHER SOURCE(S): MARPAT 135:195577
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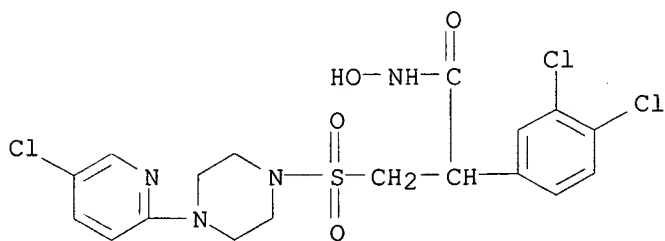
AB The title compds. [I; B = (un)substituted Ph, 2-pyridyl, 2-pyridyloxy, 4-pyrimidinyl; X = C, N; R1 = (trimethyl-1-hydantoin)alkyl, (un)substituted Ph, phenylalkyl, etc.], useful as metalloproteinase inhibitors, esp. as inhibitors of MMP 13, were prepd. E.g., a 5-step synthesis of I [B = 4-FC6H4; X = CH; R1 = CH2Ph] was given.
 IT **357187-74-7P 357187-78-1P 357187-79-2P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of arylpiperazines and arylpiperidines as metalloproteinase inhibiting agents)
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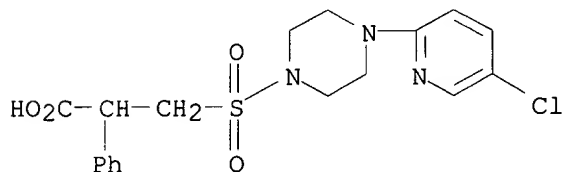
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RN 357187-79-2 HCAPLUS
 CN Benzeneacetamide, 3,4-dichloro-.alpha.-[[[4-(5-chloro-2-pyridinyl)-1-piperazinyl]sulfonyl]methyl]-N-hydroxy- (9CI) (CA INDEX NAME)



IT 357187-91-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of arylpiperazines and arylpiperidines as metalloproteinase inhibiting agents)
 RN 357187-91-8 HCAPLUS
 CN Benzeneacetic acid, .alpha.-[[[4-(5-chloro-2-pyridinyl)-1-piperazinyl]sulfonyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L16 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:636059 HCAPLUS

DOCUMENT NUMBER: 135:211053

TITLE: Preparation of N-[2-(piperidino- or piperazino)sulfonylethyl]-N-hydroxyformamides as inhibitors of metalloproteinases

INVENTOR(S): Barlaam, Bernard Christophe; Dowell, Robert Ian; Finlay, Maurice Raymond Verschoyle; Newcombe, Nicholas John; Tucker, Howard; Waterson, David

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

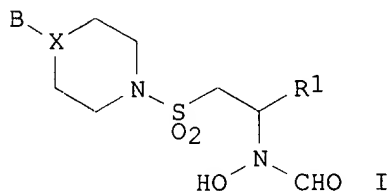
FAMILY ACC. NUM. COUNT: 1

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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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NO 2002003956	A	20021007	NO 2002-3956	20020820
PRIORITY APPLN. INFO.:			EP 2000-400467	A 20000221
			WO 2001-GB624	W 20010215

OTHER SOURCE(S): MARPAT 135:211053

GI



AB The title compds. [I; B = (un)substituted Ph, 2-pyridyl, 2-pyridyloxy, 4-pyrimidinyl; X = CH, N; R1 = phenylalkyl, pyridylalkyl, pyrimidinylalkyl, etc.], useful as metalloproteinase inhibitors, esp. as inhibitors of MMP 13 (no data given), were prepd. E.g., a 4-step synthesis of I [B = 4-BrC6H4; X = N; R1 = 3-(pyrimidin-2-yl)propyl] was given. The compds. I are effective at 0.5-30 mg/kg/day.

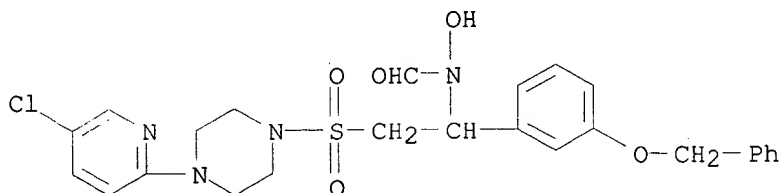
IT 357645-52-4P 357645-55-7P 357645-57-9P
357645-58-0P 357646-20-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-[2-(piperidino- or piperazino)sulfonyl]ethyl]-N-hydroxyformamides as inhibitors of metalloproteinases)

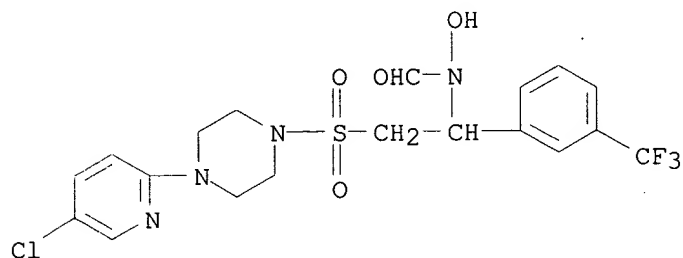
RN 357645-52-4 HCAPLUS

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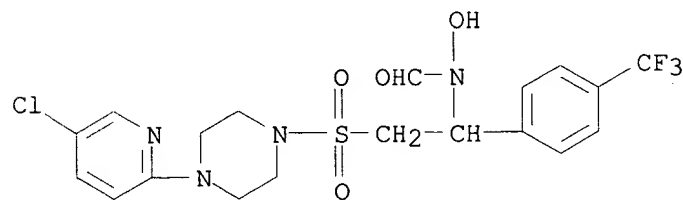
RN 357645-55-7 HCAPLUS

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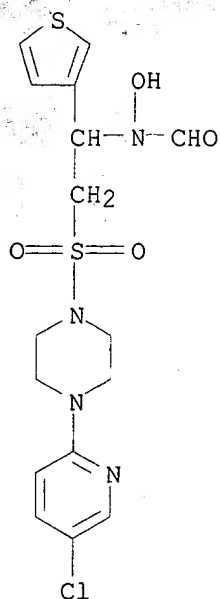
RN 357645-57-9 HCAPLUS

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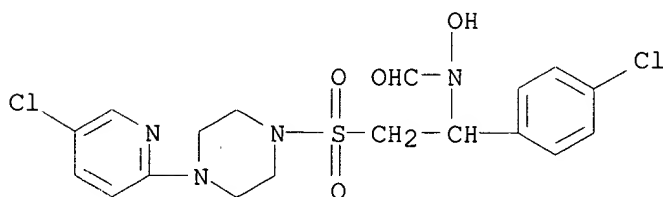


RN 357645-58-0 HCAPLUS

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RN 357646-20-9 HCAPLUS
 CN Piperazine, 1-[[2-(4-chlorophenyl)-2-(formylhydroxyamino)ethyl]sulfonyl]-4-(5-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L16 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:161258 HCAPLUS

DOCUMENT NUMBER: 132:207849

TITLE: Preparation of arylpiperazines as metalloproteinase inhibiting agents (MMP)

INVENTOR(S): Barlaam, Bernard Christophe; Newcombe, Nicholas John; Tucker, Howard; Waterson, David

PATENT ASSIGNEE(S): Zeneca Limited, UK; Zeneca-Pharma Sa

SOURCE: PCT Int. Appl., 82 pp.

CODEN: PIXXD2

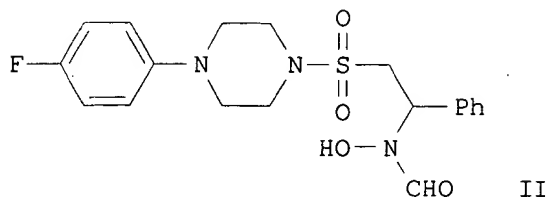
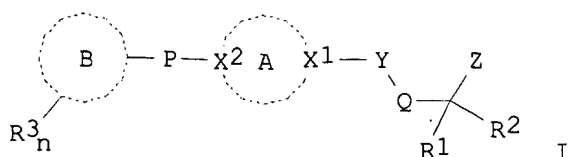
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LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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EP 1109787	A1	20010627	EP 1999-941751	19990825
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PRIORITY APPLN. INFO.:			EP 1998-402144	A 19980831
			EP 1999-401351	A 19990604
			WO 1999-GB2801	W 19990825
OTHER SOURCE(S):	MARPAT 132:207849			
GI				



AB The title compds. [I; B = monocyclic or bicyclic alkyl, aryl, etc.; R3 = H, halo, NO2. etc.; n = 1-3; P = (CH2)_n (wherein n = 0-2), alkene, alkyne, etc.; A = (un)substituted 5-7 membered aliph. ring; X1, X2 = N, C, where a ring substituent on ring A is a oxo group that is preferably adjacent a ring N atom; Y = SO2, CO; Z = CONHOH, Y = CO and Q = CR6R7, CR6R7CH2, NR6, NR6CH2 (wherein R6 = H, alkyl, aralkyl, etc.; R7 = H, alkyl; R7 together with R6 forms a carbocyclic or heterocyclic spiro 5-7 membered ring, the latter contg. at least one heteroatom selected from N, O, S); Z = CONHOH, Y = SO2 and Q = CR6R7, CR6R7CH2; Z = N(OH)CHO and Q = CHR6, CHR6CH2, NR6CH2; R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, aryl, etc.], useful as metalloproteinase inhibitors (no data), esp. as inhibitors of MMP 13, in treating arthritis and atherosclerosis, were prepd. E.g., a multi-step synthesis of the title piperazine II was given. Compds. I are effective at 0.5-30 mg/kg/day.

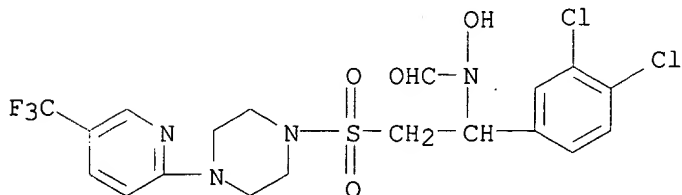
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of arylpiperazines as metalloproteinase inhibiting agents (MMP))

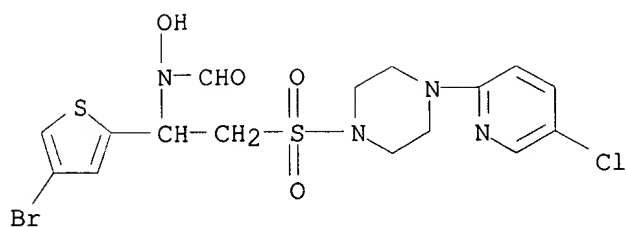
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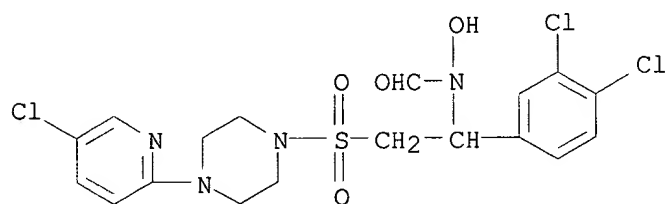
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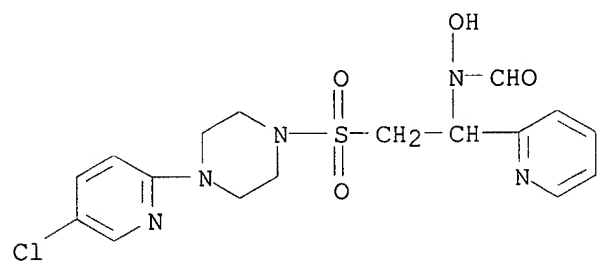
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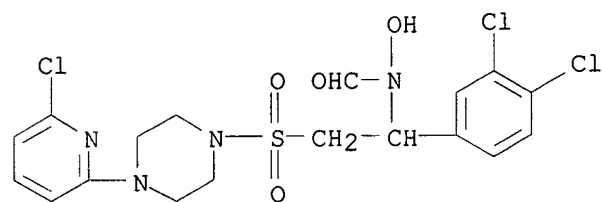
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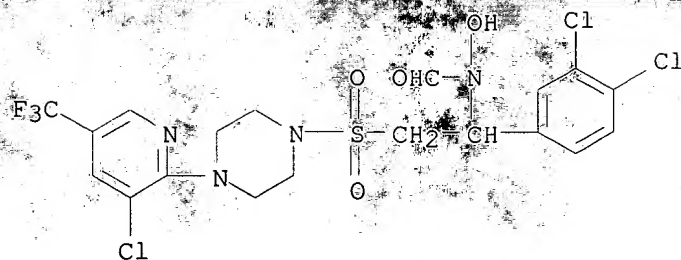
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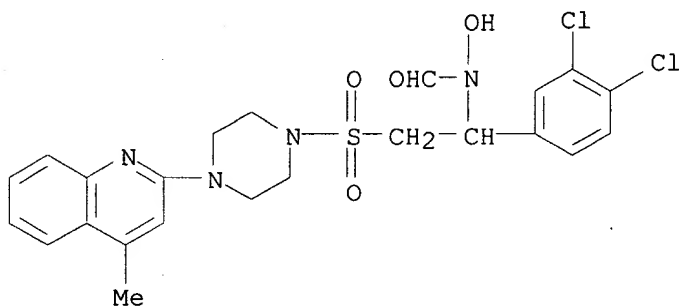
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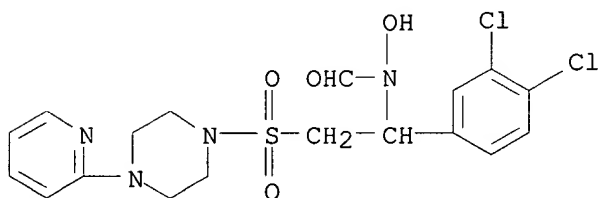
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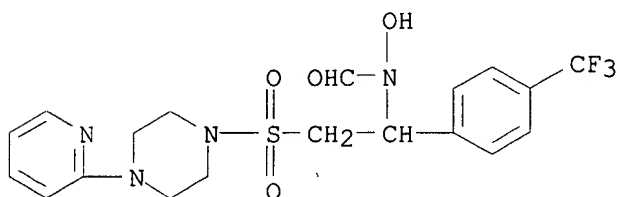
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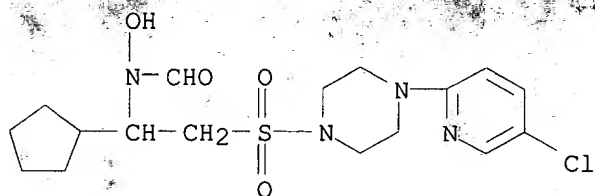
RN 260439-18-7 HCAPLUS

CN Piperazine, 1-[[2-(formylhydroxyamino)-2-[4-(trifluoromethyl)phenyl]ethyl]sulfonyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)

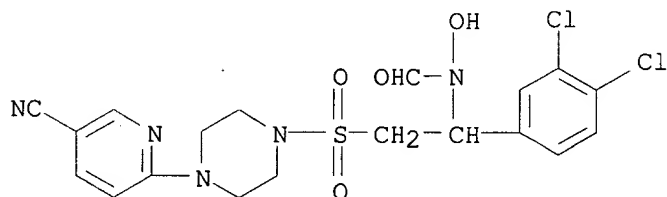


RN 260439-31-4 HCAPLUS

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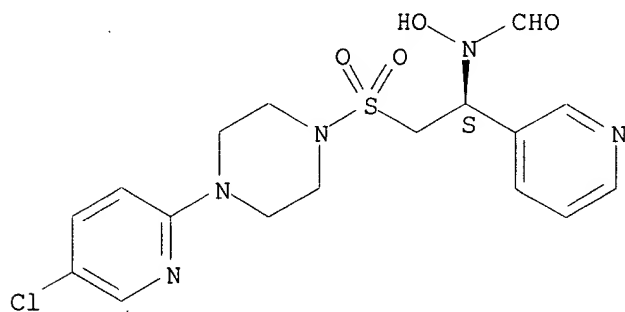


RN 260439-32-5 HCAPLUS
 CN Piperazine, 1-(5-cyano-2-pyridinyl)-4-[[2-(3,4-dichlorophenyl)-2-(formylhydroxyamino)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

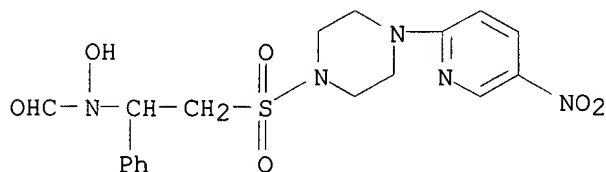


RN 260439-80-3 HCAPLUS
 CN Piperazine, 1-(5-chloro-2-pyridinyl)-4-[[2-(3,4-dichlorophenyl)-2-(formylhydroxyamino)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

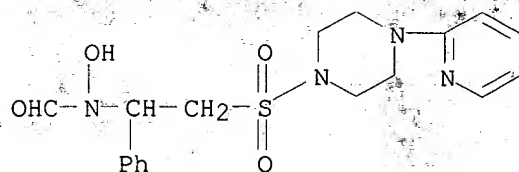
Absolute stereochemistry.



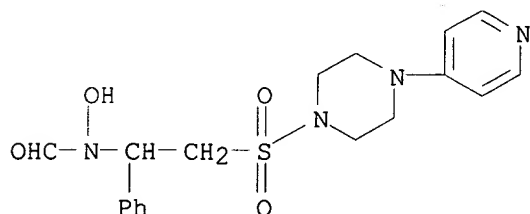
RN 260440-05-9 HCAPLUS
 CN Piperazine, 1-[[2-(formylhydroxyamino)-2-phenylethyl]sulfonyl]-4-(5-nitro-2-pyridinyl)- (9CI) (CA INDEX NAME)



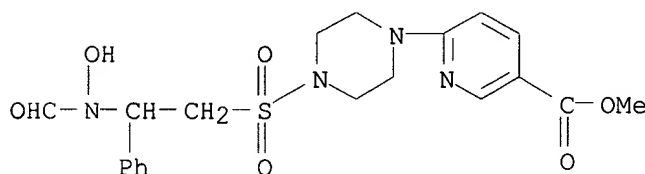
RN 260440-10-6 HCAPLUS
 CN Piperazine, 1-[[2-(formylhydroxyamino)-2-phenylethyl]sulfonyl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)



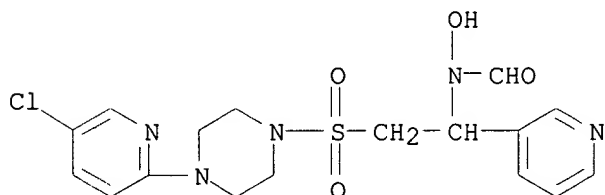
RN 260440-19-5 HCAPLUS
 CN Piperazine, 1-[[2-(formylhydroxyamino)-2-phenylethyl]sulfonyl]-4-(4-pyridinyl)- (9CI) (CA INDEX NAME)



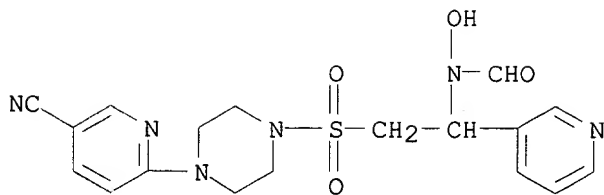
RN 260440-23-1 HCAPLUS
 CN 3-Pyridinecarboxylic acid, 6-[4-[[2-(formylhydroxyamino)-2-phenylethyl]sulfonyl]-1-piperazinyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 260440-57-1 HCAPLUS
 CN Piperazine, 1-(5-chloro-2-pyridinyl)-4-[[2-(formylhydroxyamino)-2-(3-pyridinyl)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

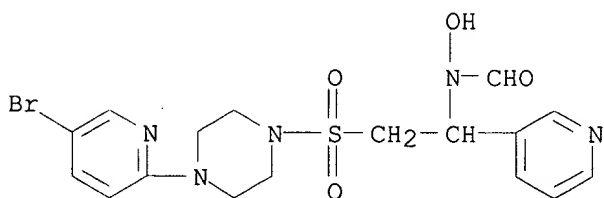


RN 260440-84-4 HCAPLUS
 CN Piperazine, 1-(5-cyano-2-pyridinyl)-4-[[2-(formylhydroxyamino)-2-(3-pyridinyl)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)



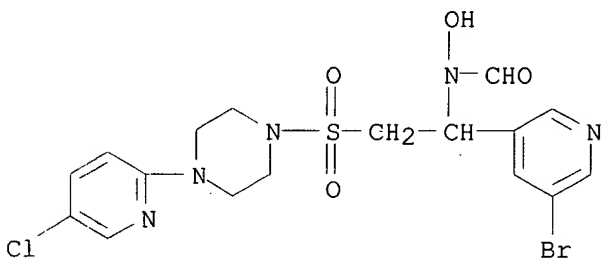
RN 260440-89-9 HCAPLUS

CN Piperazine, 1-(5-bromo-2-pyridinyl)-4-[[2-(formylhydroxyamino)-2-(3-pyridinyl)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 260440-99-1 HCAPLUS

CN Piperazine, 1-[[2-(5-bromo-3-pyridinyl)-2-(formylhydroxyamino)ethyl]sulfonyl]-4-(5-chloro-2-pyridinyl)- (9CI) (CA INDEX NAME)

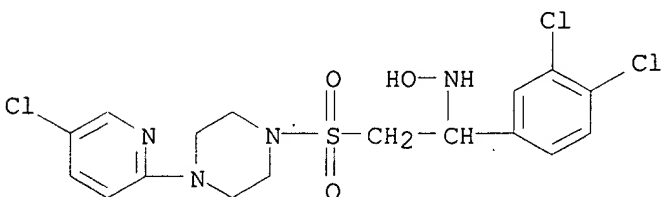


IT 260441-75-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of arylpiperazines as metalloproteinase inhibiting agents
(MMP))

RN 260441-75-6 HCAPLUS

CN Piperazine, 1-(5-chloro-2-pyridinyl)-4-[[2-(3,4-dichlorophenyl)-2-(hydroxyamino)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

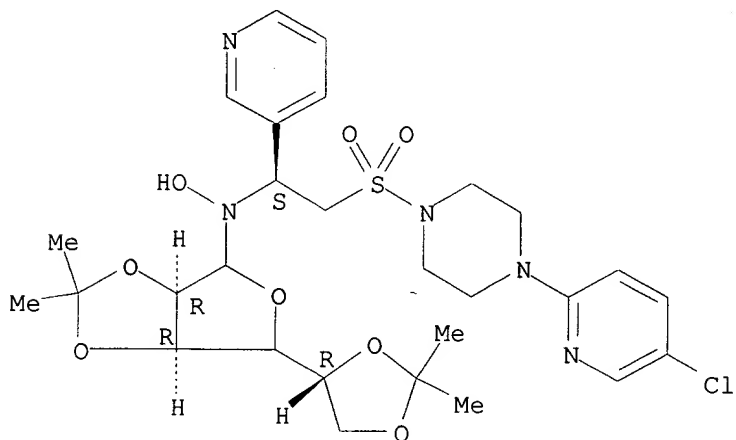


IT 260441-62-1P 260441-63-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of arylpiperazines as metalloproteinase inhibiting agents
(MMP))

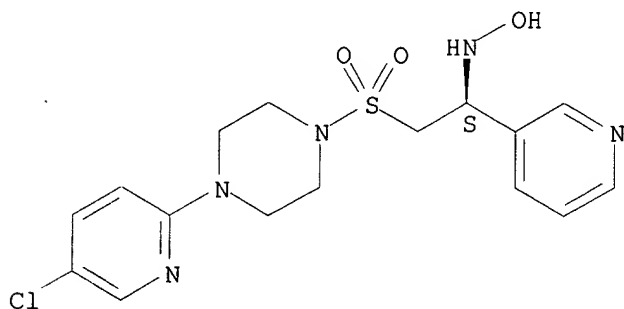
RN 260441-62-1 HCAPLUS
 CN Piperazine, 1-[[[(2S)-2-[[[(4.xi.)-2,3:5,6-bis-O-(1-methylethylidene)-D-ribo-
 hexofuranosyl]hydroxyamino]-2-(3-pyridinyl)ethyl]sulfonyl]-4-(5-chloro-2-
 pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260441-63-2 HCAPLUS
 CN Piperazine, 1-(5-chloro-2-pyridinyl)-4-[[[(2S)-2-(hydroxyamino)-2-(3-
 pyridinyl)ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 116 4

L16 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:6879 HCAPLUS

DOCUMENT NUMBER: 124:176036

TITLE: Design, Synthesis, and Structure-Activity Relationship Studies of Novel 1-[(1-Acyl-4-piperidinyl)methyl]-1H-2-methylimidazo[4,5-c]pyridine Derivatives as Potent, Orally Active Platelet-Activating Factor Antagonists

AUTHOR(S): Carceller, Elena; Merlos, Manuel; Giral, Marta; Balsa, Dolores; Garcia-Rafanell, Julian; Forn, Javier

CORPORATE SOURCE: Research Center, J. Uriach Cia. S.A., Barcelona, 08026, Spain

SOURCE: Journal of Medicinal Chemistry (1996), 39(2), 487-93
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

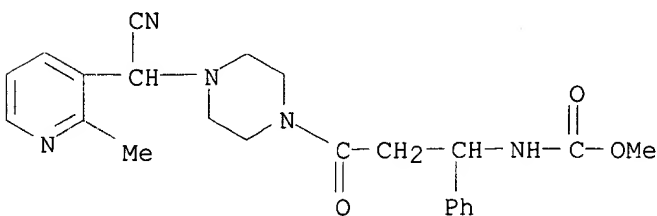
AB Replacement of the polar head of the previously reported series of 1-acyl-4-[(2-methyl-3-pyridyl)cyanomethyl]piperazines with a 2-methylimidazo[4,5-c]pyridine group led to the identification of a new series of 1-[(1-acyl-4-piperidinyl)methyl]-1H-2-methylimidazo[4,5-c]pyridine derivs. as potent, orally active platelet-activating factor (PAF) antagonists. On the basis of the general structure-activity relationship trends found for the acyl substituent in our earlier series, five groups of compds. were tested, i.e., diaryl- or alkylarylpropanoyl derivs., their 3-hydroxy-substituted analogs, and urea, carbamate and amino acid derivs. The optimal compd. UR-12670, bearing the 3,3-diphenylpropanoyl moiety, exhibited very high in vitro and in vivo potency (IC₅₀ = 0.0076 .mu.M for the in vitro PAF-induced platelet aggregation assay, ID₅₀ = 0.0086 mg/kg for the in vivo PAF-induced hypotension test in normotensive rats, and ID₅₀ = 0.092 mg/kg po and 0.0008 mg/kg i.v. for the PAF-induced mortality test in mice). UR-12670 also showed long duration of activity. It gave 100% protection against PAF-induced mortality in mice 7 h after i.v. administration of a single dose of 1 mg/kg and also provided 100% inhibition of PAF-induced aggregation in dog whole blood 6 h after i.v. administration of the same dose. The lead structure UR-12670 was selected for in-depth pharmacol. evaluation.

IT 149692-09-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structure activity relationship of (piperidinyl)methyl]imidazo[4,5-c]pyridines as platelet activating factor antagonists)

RN 149692-09-1 HCAPLUS

CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, methyl ester (9CI) (CA INDEX NAME)



=> d ibib abs hitstr 116 5

L16 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1995:380148 HCAPLUS
 DOCUMENT NUMBER: 122:160682
 TITLE: Cyanomethylpyridine derivatives as PAF antagonists and
 5-lipoxygenase inhibitors
 INVENTOR(S): Carceller, Elena; Jimenez, Pere J.; Almansa, Carmen;
 Bartoli, Javier
 PATENT ASSIGNEE(S): J. Uriach y Cia. S.A., Spain
 SOURCE: Eur. Pat. Appl., 25 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 617032	A1	19940928	EP 1994-104612	19940323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ES 2062943	A1	19941216	ES 1993-591	19930323
ES 2062943	B1	19951116		
CA 2118831	AA	19940924	CA 1994-2118831	19940311
JP 07002841	A2	19950106	JP 1994-76436	19940323
US 5420131	A	19950530	US 1994-216583	19940323
PRIORITY APPLN. INFO.:			ES 1993-591	19930323
OTHER SOURCE(S):		MARPAT 122:160682		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

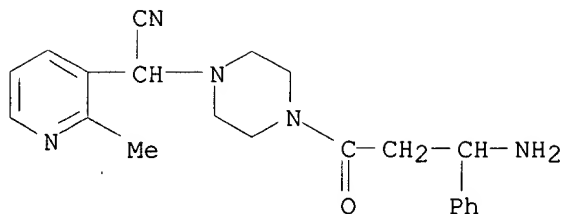
AB The invention relates to cyanomethylpyridine derivs. I [Y = N or CH; R1 = F, Cl; R2 = H or Cl-4 alkyl; m = 0, 1 or 2; n = 0 or 1; p = 0 or 1; A = covalent bond, CONHCH(Ar), NHCH(Ar), SO2NHCH(Ar), NHCONHCH(Ar), or OCONHCH(Ar); and when p = 1, A can also = CH(Ar)NH; Ar = Ph or Ph substituted .gtoreq. 1 of halo, Cl-4 alkyl, Cl-4 alkoxy, or CF3]. The compds. are platelet activating factor (PAF) antagonists and/or 5-lipoxygenase inhibitors, and are useful for treating a variety of diseases. For example, coupling of p-(2-quinolylmethoxy)phenylacetic acid with 1-(3-amino-3-phenylpropionyl)-4-[(2-methyl-3-pyridyl)cyanomethyl]piperazine using DCC and 1-hydroxybenzotriazole in DMF gave 43% title compd. II, a preferred compd. The IC50 of II for inhibition of PAF-induced hypotension in normotensive rats was 0.036 mg/kg i.v. Twelve addnl. syntheses, addnl. biol. tests (inhibition of PAF-induced platelet aggregation, and inhibition of LTB4 prodn.), and 6 example formulations are given.

IT 149691-83-8

RL: RCT (Reactant); RACT (Reactant or reagent)
 (amidation; prepn. of cyanomethylpyridine derivs. as PAF antagonists and 5-lipoxygenase inhibitors)

RN 149691-83-8 HCAPLUS

CN 1-Piperazineacetonitrile, 4-(3-amino-1-oxo-3-phenylpropyl)-.alpha.-(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



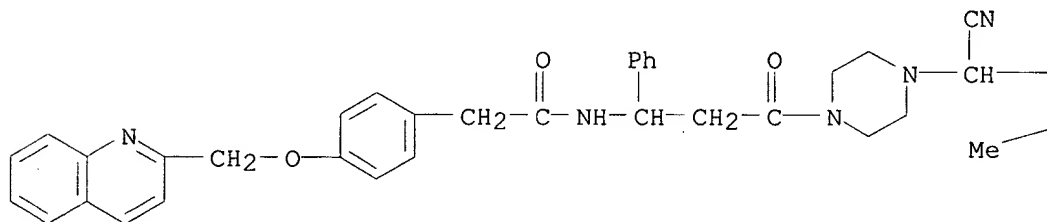
IT 161180-94-5P 161180-95-6P 161180-96-7P
161180-97-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cyanomethylpyridine derivs. as PAF antagonists and 5-lipoxygenase inhibitors)

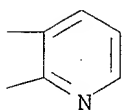
RN 161180-94-5 HCAPLUS

CN Benzeneacetamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-4-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)

PAGE 1-A



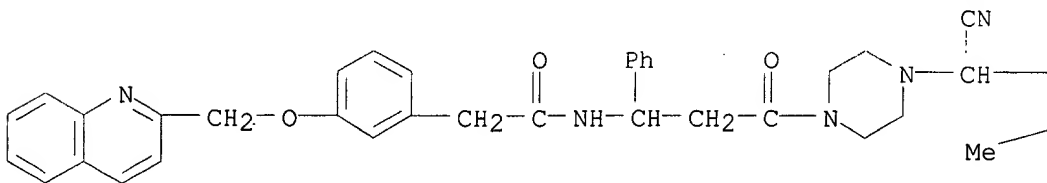
PAGE 1-B

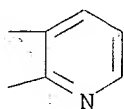


RN 161180-95-6 HCAPLUS

CN Benzeneacetamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-3-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)

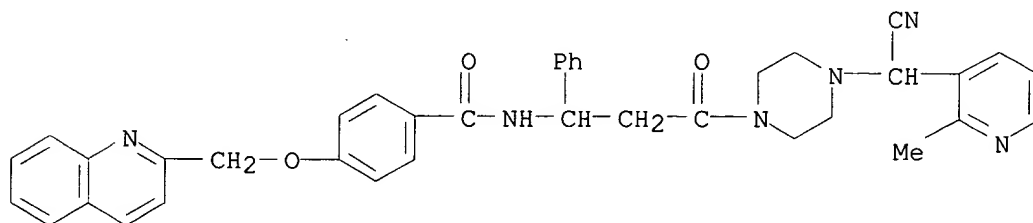
PAGE 1-A





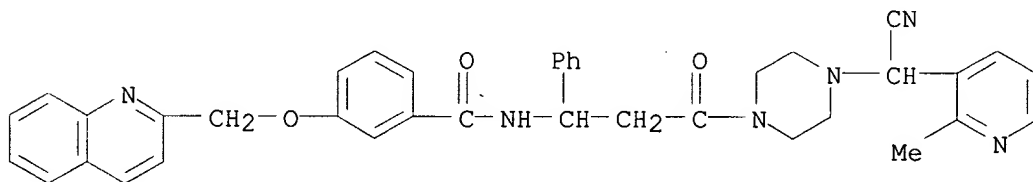
RN 161180-96-7 HCAPLUS

CN Benzamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-4-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)



RN 161180-97-8 HCAPLUS

CN Benzamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-3-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)



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L16 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:106931 HCAPLUS

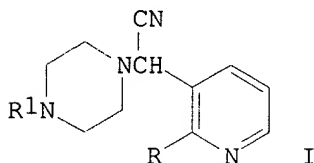
DOCUMENT NUMBER: 120:106931

TITLE: Synthesis and structure-activity relationships of
1-acyl-4-((2-methyl-3-pyridyl)cyanomethyl)piperazines
as PAF antagonistsAUTHOR(S): Carceller, Elena; Merlos, Manuel; Giral, Marta;
Almansa, Carmen; Bartroli, Javier; Garcia-Rafanell,
Julian; Forn, JavierCORPORATE SOURCE: Chem. Lab., J. Uriach e Cia.S.A., Barcelona, 08026,
SpainSOURCE: Journal of Medicinal Chemistry (1993), 36(20), 2984-97
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



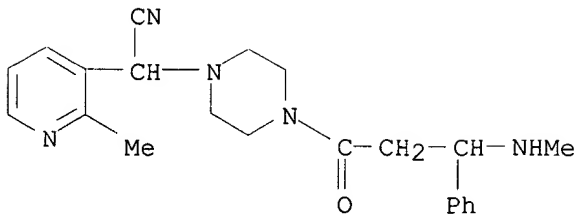
AB Title compds., e.g. I [R = Me, R1 = Ph2CHXCH2CO, PhCR2R3CH2CO, R4NHCHPhCO; X = CH2, CH2CH2, NH, NCHO, NAc, NSO2Me, O, S(O), SO2; R2 = OH, CO2Et, F, R3 = Ph, Me, CF3, 3-pyridyl; R4 = PhO2C, PhCH2O2C, MeO2C, EtO2C, Me2CHCH2O2C, Me3CO2C, H2NCO, pyrrolidinocarbonyl, Bz, 3-pyridylcarbonyl, 3-furylcarbonyl, 2-piperazinylcarbonyl, Ac, Me, PhSO2, MeSO2, H, Ph, PhCH2, 3-pyridylmethyl, H2C:CHCH2, HC.tplbond.CCH2], second generation (cyanomethyl)piperazines with increased oral activity were prepd. and evaluated in vitro in a platelet aggregation factor (PAF)-induced platelet aggregation assay and in vivo in a PAF-induced hypotension test in normotensive rats. Oral activity was ascertained through a PAF-induced mortality test in mice. I (R = Me) showed an order of magnitude or greater improvement in the oral ID50 test compared with I (R = H). Three different types of acyl substituents of similar potency emerge from this work: R1 = Ph2CHNHCH2CO, HOCR3PhCH2CO, and R4NHCHPhCH2CO. The most interesting compds., I (R = Me, R1 = Ph2CHNHCH2CO) (II) (UR-12460) and I (R = Me, R1 = MeO2CNHCHPhCH2CO) (UR-12519) (III) compare favorably with WEB-2086. II and III were also tested in active anaphylactic shock and endotoxin-induced mortality tests. On the basis of these data and addnl. pharmacol. development, II and III were selected for clin. testing.

IT 149692-22-8 149692-25-1

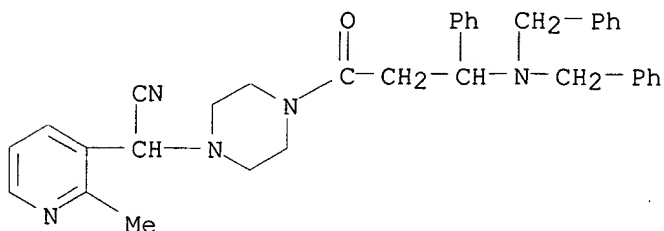
RL: RCT (Reactant); RACT (Reactant or reagent)
(platelet aggregation factor antagonistic activity of)

RN 149692-22-8 HCAPLUS

CN 1-Piperazineacetonitrile, 4-[3-(methylamino)-1-oxo-3-phenylpropyl]-.alpha.-
(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



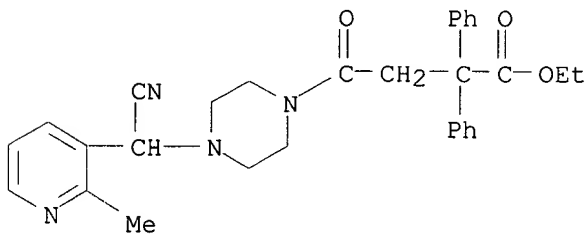
RN 149692-25-1 HCAPLUS
 CN 1-Piperazineacetonitrile, 4-[3-[bis(phenylmethyl)amino]-1-oxo-3-phenylpropyl]-.alpha.-(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



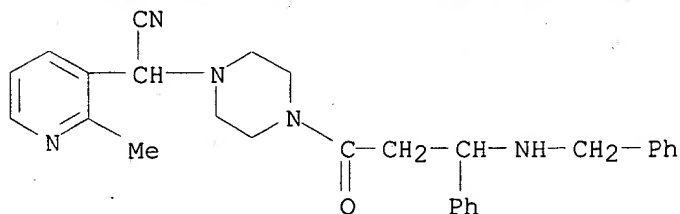
IT 149691-77-0P 149691-84-9P 149691-85-0P
 149691-86-1P 149692-10-4P 149692-11-5P
 149692-12-6P 149692-13-7P 149692-14-8P
 149692-15-9P 149692-16-0P 149692-17-1P
 149692-18-2P 149692-20-6P 149692-21-7P
 149692-24-0P 149692-26-2P 149692-27-3P
 149692-28-4P 149692-29-5P 149692-30-8P
 149692-31-9P 149692-41-1P 150812-47-8P
 150812-48-9P 150812-49-0P 150812-50-3P
 150812-51-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and platelet aggregation factor antagonistic activity of)

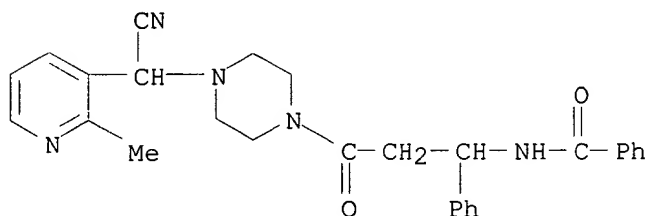
RN 149691-77-0 HCAPLUS
 CN 1-Piperazinebutanoic acid, 4-[cyano(2-methyl-3-pyridinyl)methyl]-.gamma.-oxo-.alpha.,.alpha.-diphenyl-, ethyl ester (9CI) (CA INDEX NAME)



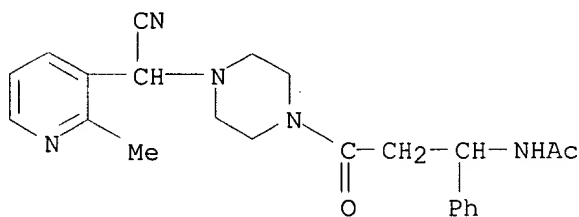
RN 149691-84-9 HCAPLUS
 CN 1-Piperazineacetonitrile, .alpha.-(2-methyl-3-pyridinyl)-4-[1-oxo-3-phenyl-3-[(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)



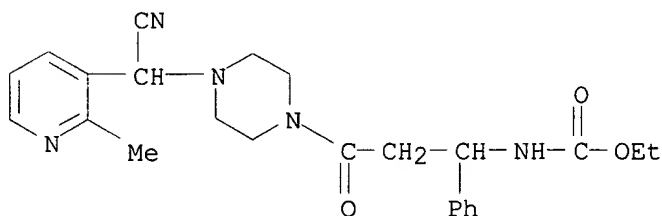
RN 149691-85-0 HCAPLUS
 CN Benzamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]- (9CI) (CA INDEX NAME)



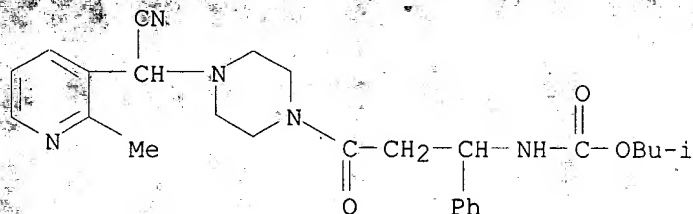
RN 149691-86-1 HCAPLUS
 CN Acetamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]- (9CI) (CA INDEX NAME)



RN 149692-10-4 HCAPLUS
 CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, ethyl ester (9CI) (CA INDEX NAME)

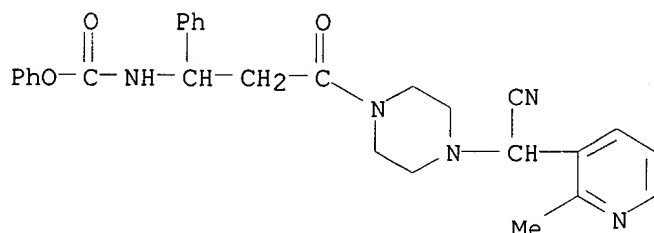


RN 149692-11-5 HCAPLUS
 CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



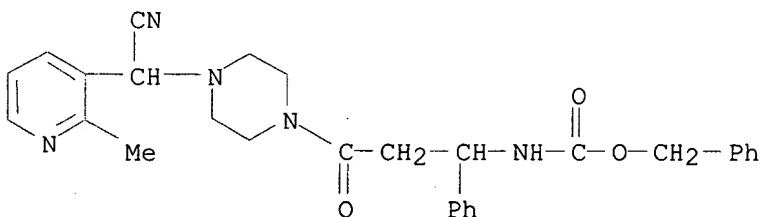
RN 149692-12-6 HCAPLUS

CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, phenyl ester (9CI) (CA INDEX NAME)



RN 149692-13-7 HCAPLUS

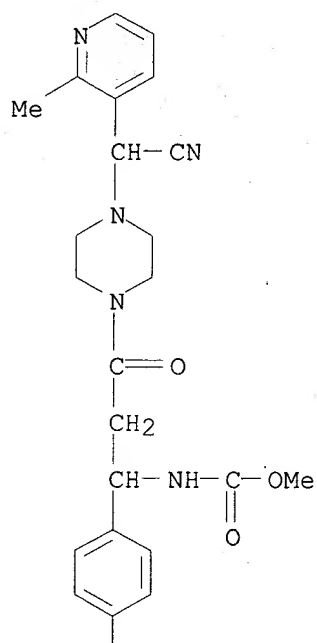
CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 149692-14-8 HCAPLUS

CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-[4-(trifluoromethyl)phenyl]propyl]-, methyl ester (9CI) (CA INDEX NAME)

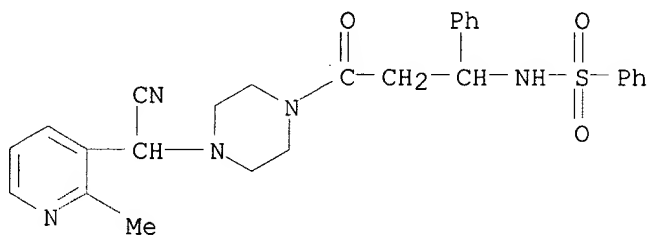
PAGE 1-A



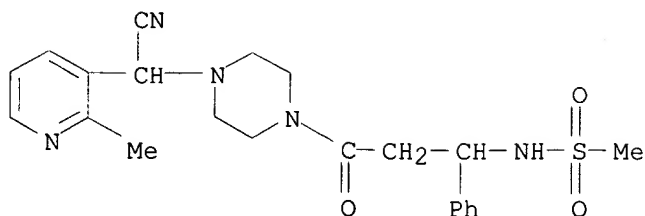
PAGE 2-A



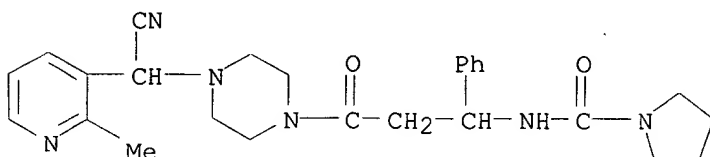
RN 149692-15-9 HCAPLUS
 CN 1-Piperazineacetonitrile, .alpha.-(2-methyl-3-pyridinyl)-4-[1-oxo-3-phenyl-3-[(phenylsulfonyl)amino]propyl]- (9CI) (CA INDEX NAME)



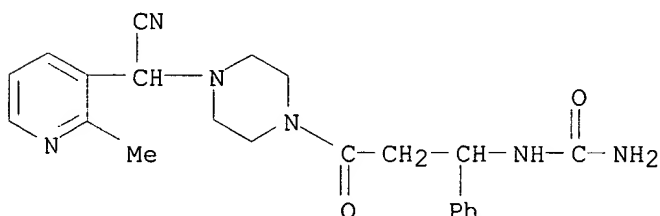
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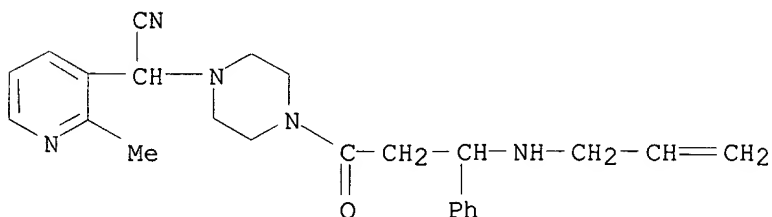
RN 149692-17-1 HCAPLUS
CN 1-Piperazinecarboxamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]- (9CI) (CA INDEX NAME)



RN 149692-18-2 HCAPLUS
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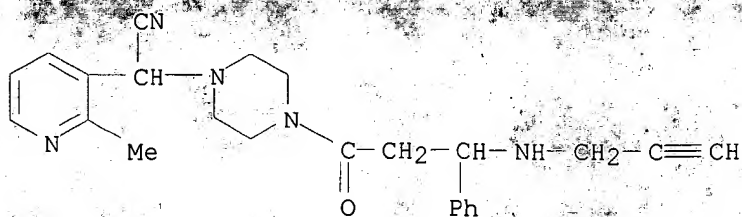


RN 149692-20-6 HCAPLUS
CN 1-Piperazinecarboxamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]- (9CI) (CA INDEX NAME)

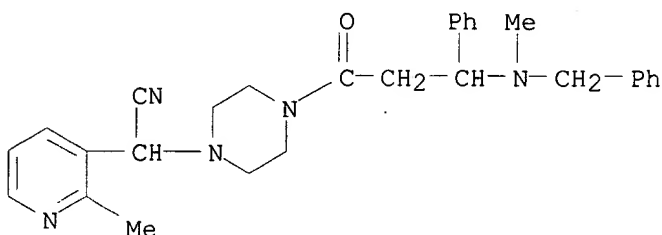


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RN 149692-21-7 HCAPLUS
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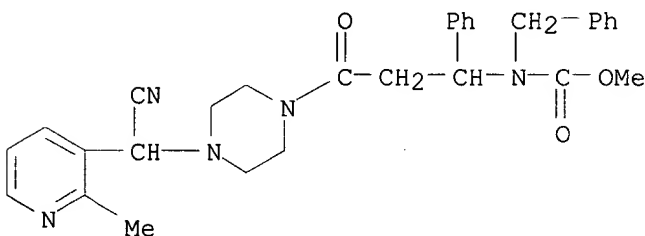


RN 149692-24-0 HCAPLUS
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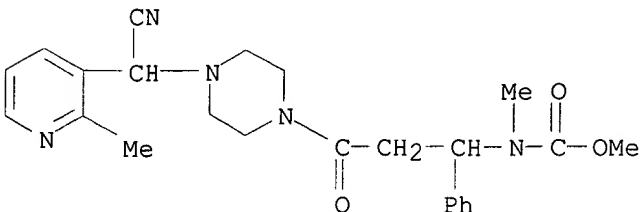


● 2 HCl

RN 149692-26-2 HCAPLUS
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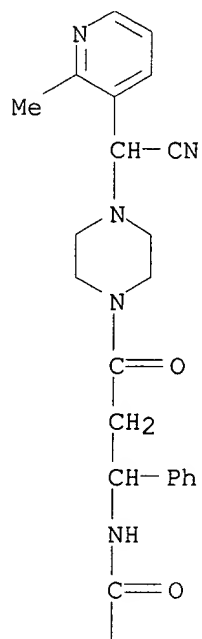
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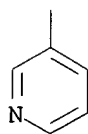
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 CN 3-Pyridinecarboxamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-

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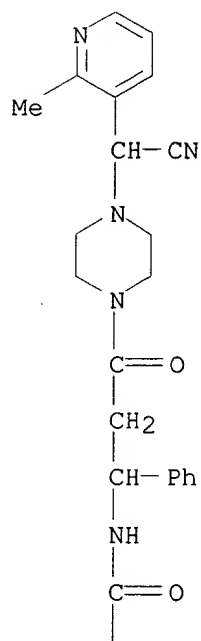


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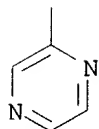


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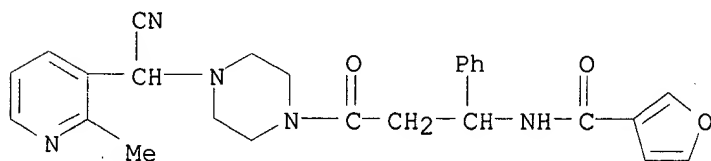
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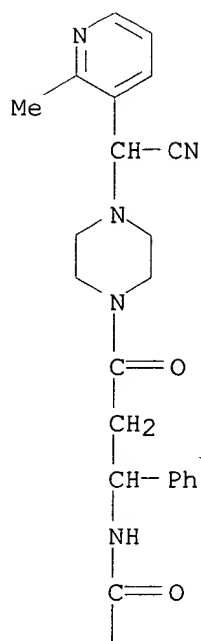


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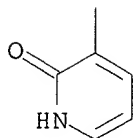


RN 149692-31-9 HCAPLUS
 CN 3-Pyridinecarboxamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-1,2-dihydro-2-oxo- (9CI) (CA INDEX NAME)

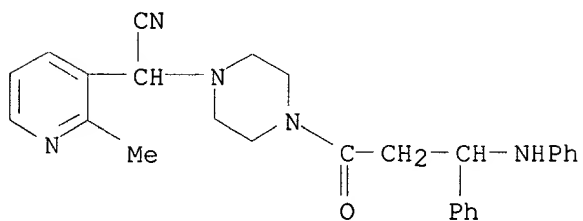
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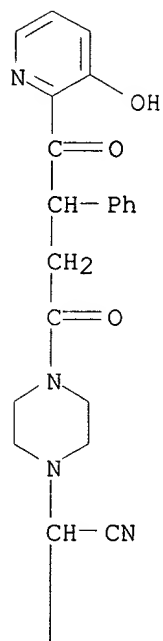


RN 149692-41-1 HCAPLUS
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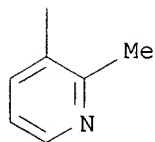


RN 150812-47-8 HCAPLUS
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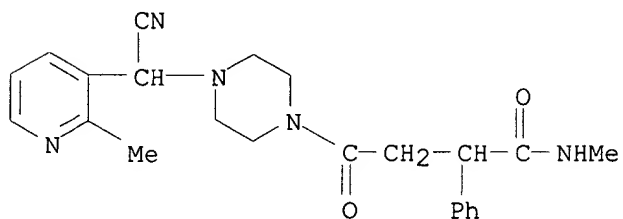
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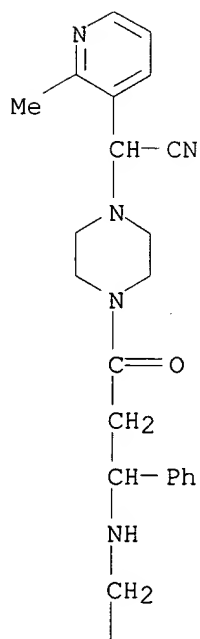


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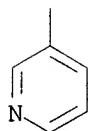


RN 150812-49-0 HCAPLUS
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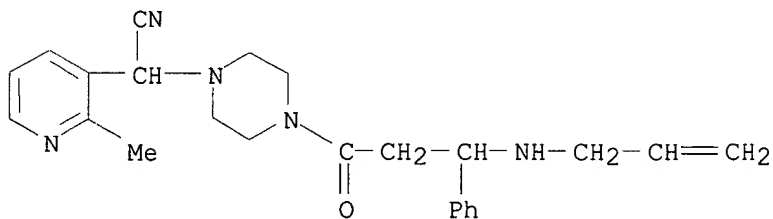
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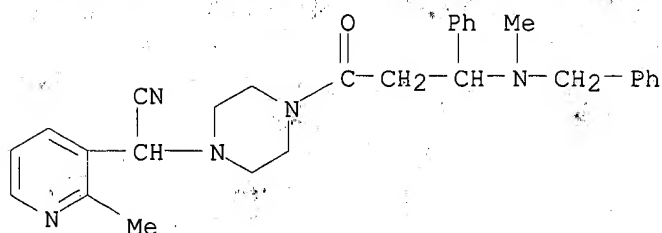
PAGE 2-A



RN 150812-50-3 HCAPLUS
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RN 150812-51-4 HCAPLUS
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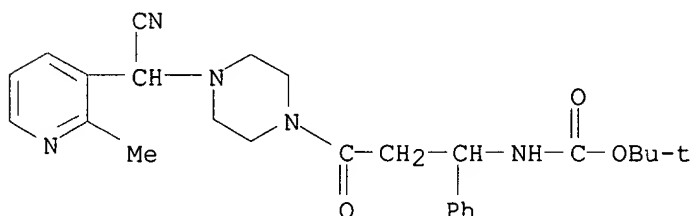


IT 149691-82-7P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., deprotection, and platelet aggregation factor antagonistic activity of)

RN 149691-82-7 HCAPLUS

CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

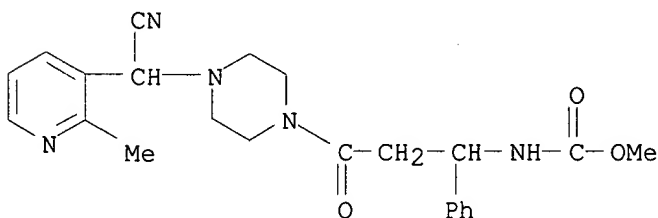


IT 149692-09-1P, UR 12519

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., platelet aggregation factor antagonistic activity, and toxicity of)

RN 149692-09-1 HCAPLUS

CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-, methyl ester (9CI) (CA INDEX NAME)

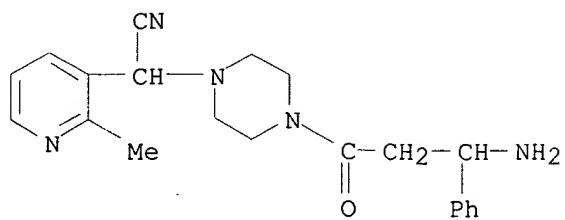


IT 149691-83-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn., reactions, and platelet aggregation factor antagonistic activity of)

RN 149691-83-8 HCAPLUS

CN 1-Piperazineacetoneitrile, 4-(3-amino-1-oxo-3-phenylpropyl)-.alpha.-(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)
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This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

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DICTIONARY FILE UPDATES: 19 MAR 2003 HIGHEST RN 500101-42-8
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TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

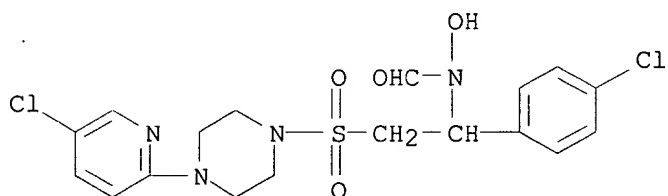
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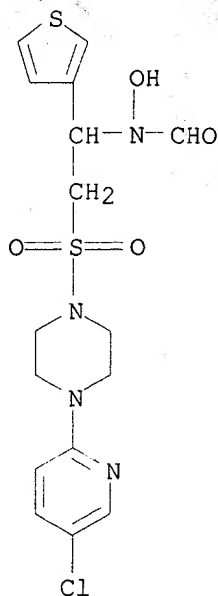


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1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:211053

L15 ANSWER 2 OF 80 REGISTRY COPYRIGHT 2003 ACS
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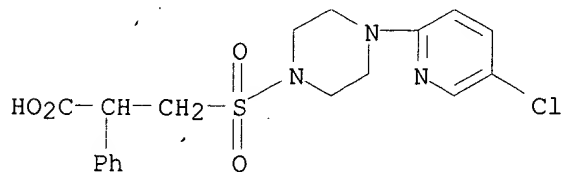


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L15 ANSWER 6 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 357187-91-8 REGISTRY
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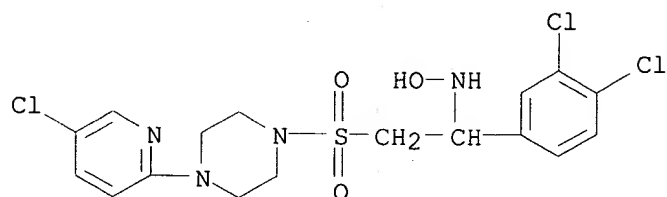
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L15 ANSWER 10 OF 80 REGISTRY COPYRIGHT 2003 ACS
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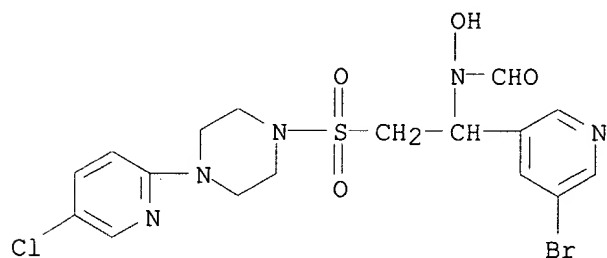


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REFERENCE 1: 132:207849

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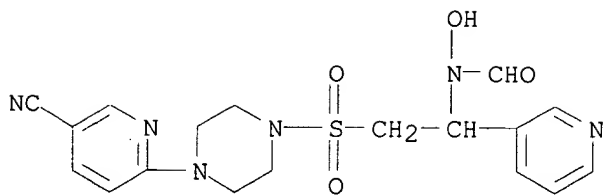


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REFERENCE 1: 132:207849

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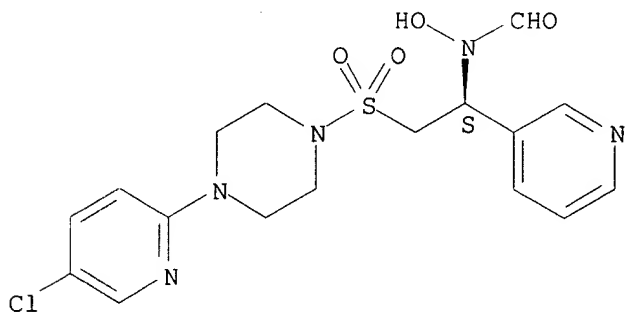
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Absolute stereochemistry.

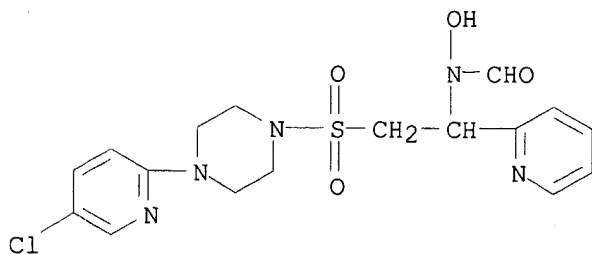


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REFERENCE 1: 132:207849

L15 ANSWER 29 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 260438-37-7 REGISTRY
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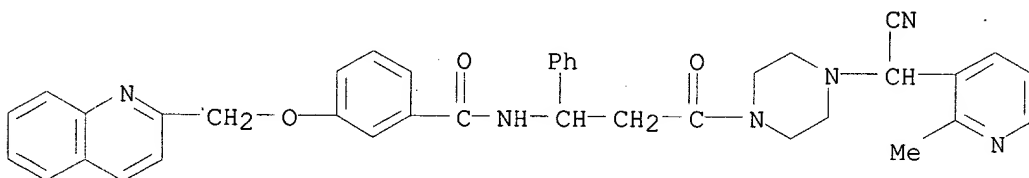


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REFERENCE 1: 132:207849

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RN 161180-97-8 REGISTRY
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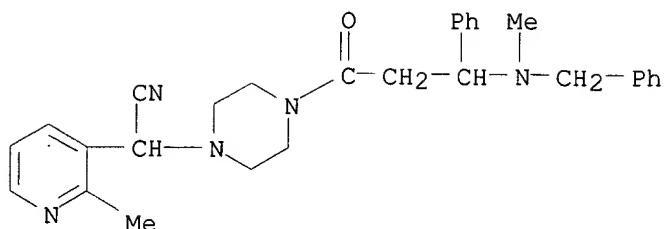


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REFERENCE 1: 122:160682

L15 ANSWER 37 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 150812-51-4 REGISTRY
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SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

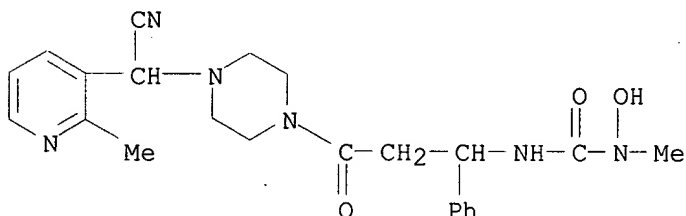


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 120:106931

L15 ANSWER 42 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 149692-45-5 REGISTRY
CN 1-Piperazineacetonitrile, 4-[3-[[(hydroxymethylamino) carbonyl] amino]-1-oxo-3-phenylpropyl]-.alpha.-(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H28 N6 O3
SR CA
LC STN Files: CA, CAPLUS

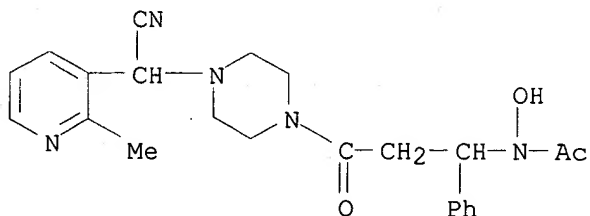


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 119:139266

L15 ANSWER 45 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 149692-42-2 REGISTRY
CN Acetamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]-N-hydroxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H27 N5 O3
SR CA
LC STN Files: CA, CAPLUS

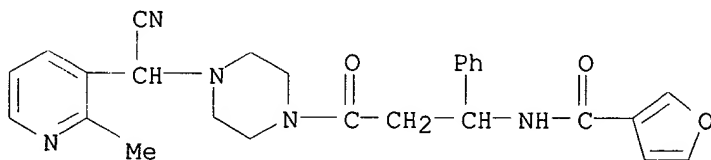


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 119:139266

L15 ANSWER 50 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 149692-30-8 REGISTRY
CN 3-Furancarboxamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H27 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



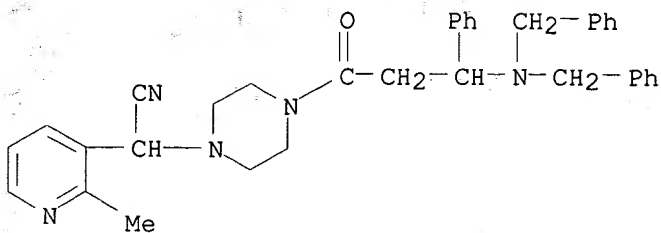
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 120:106931

REFERENCE 2: 119:139266

L15 ANSWER 55 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 149692-25-1 REGISTRY
CN 1-Piperazineacetoneitrile, 4-[3-[bis(phenylmethyl)amino]-1-oxo-3-phenylpropyl]-.alpha.-(2-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C35 H37 N5 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)

2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 120:106931

REFERENCE 2: 119:139266

L15 ANSWER 60 OF 80 REGISTRY COPYRIGHT 2003 ACS

RN 149692-19-3 REGISTRY

CN 1-Piperazineacetonitrile, .alpha.-(2-methyl-3-pyridinyl)-4-[1-oxo-3-phenyl-3-[(2-pyridinylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

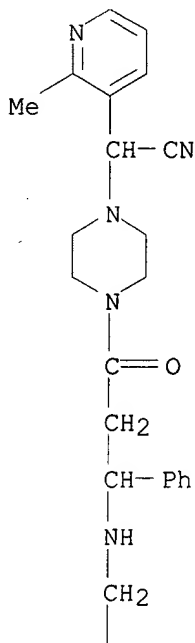
FS 3D CONCORD

MF C27 H30 N6 O

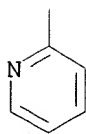
SR CA

LC STN Files: CA, CAPLUS

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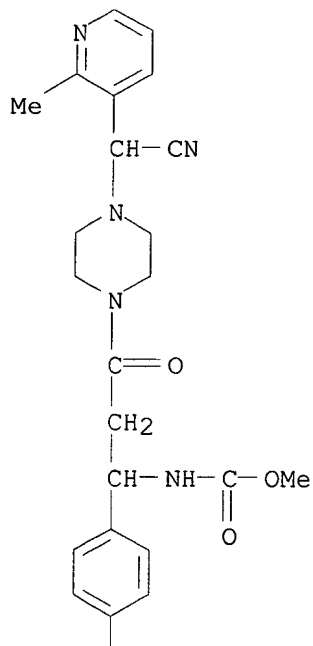
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 119:139266

L15 ANSWER 65 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 149692-14-8 REGISTRY
CN Carbamic acid, [3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-[4-(trifluoromethyl)phenyl]propyl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H26 F3 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

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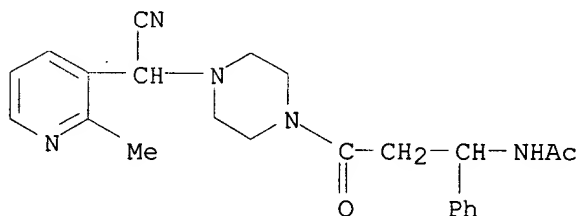
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 120:106931

REFERENCE 2: 119:139266

L15 ANSWER 71 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 149691-86-1 REGISTRY
CN Acetamide, N-[3-[4-[cyano(2-methyl-3-pyridinyl)methyl]-1-piperazinyl]-3-oxo-1-phenylpropyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H27 N5 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

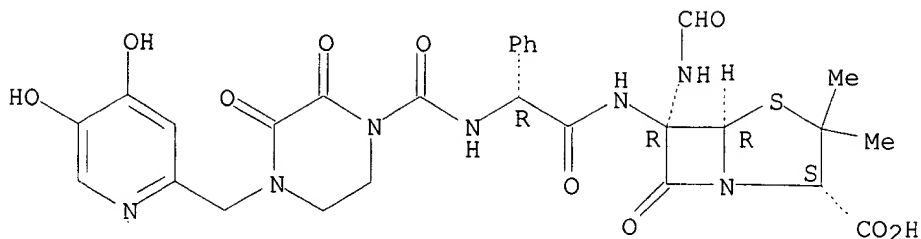
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 120:106931

REFERENCE 2: 119:139266

L15 ANSWER 77 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 121118-99-8 REGISTRY
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[4-[(4,5-dihydroxy-2-pyridinyl)methyl]-2,3-dioxo-1-piperazinyl]carbonyl]amino]phenylacetyl]amino]-6-(formylamino)-3,3-dimethyl-7-oxo-, monosodium salt, [2S-[2.alpha.,5.alpha.,6.beta.(S*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H29 N7 O10 S . Na
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
CRN (121102-21-4)

Absolute stereochemistry.



● Na

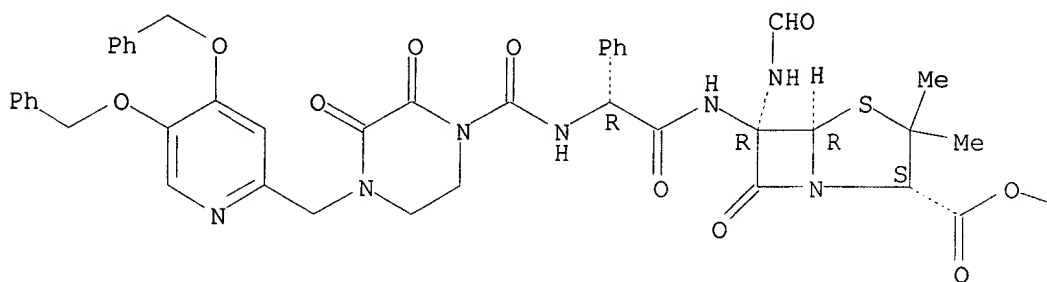
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 111:39092

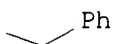
L15 ANSWER 78 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 121102-36-1 REGISTRY
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[[[4-[[4,5-bis(phenylmethoxy)-2-pyridinyl]methyl]-2,3-dioxo-1-piperazinyl]carbonyl]amino]phenylacetyl]amino]-6-(formylamino)-3,3-dimethyl-7-oxo-, phenylmethyl ester, [2S-[2.alpha.,5.alpha.,6.beta.(S*)]]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C49 H47 N7 O10 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

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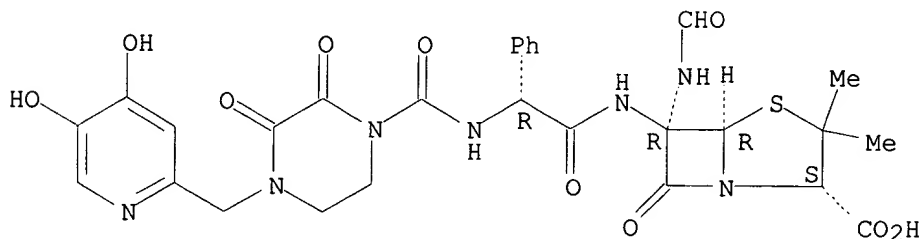
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 111:39092

L15 ANSWER 80 OF 80 REGISTRY COPYRIGHT 2003 ACS
RN 121102-21-4 REGISTRY
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[[[4-[(4,5-dihydroxy-2-pyridinyl)methyl]-2,3-dioxo-1-piperazinyl]carbonyl]amino]phenylacetyl]amino]-6-(formylamino)-3,3-dimethyl-7-oxo-, [2S-[2.alpha.,5.alpha.,6.beta.(S*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H29 N7 O10 S
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 111:39092